4/1269

Access DB# _____

SEARCH REQUEST FORM

CRFE

Scientific and Technical Information Center

Requester's Full Name: Iesha Fields Examiner #: 77985 Date: 4-30-01
Art Unit: 1645 Phone Number 30 6-5-1208 Serial Number: 09/508967
Mail Box and Bldg/Room Location: 8E-12 Results Format Preferred (circle): PAPER DISK E-MAIL
→ 8A-13

If mor than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Malaria Polypeptides

Inventors (please provide full names): Wahlgren, Mats et al

Earliest Priority Filing Date: 09/18/~~98~~97

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search SEQ ID #1

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STAFF USE ONLY	Type of Search	Vendors and cost where applicable
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Searcher Phone #: 308-4292	AA Sequence (#) 1	Dialog _____
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Date Searcher Picked Up: _____	Bibliographic _____	Dr.Link _____
Date Completed: 5/4	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: 5	Fulltext _____	Sequence Systems Compugen
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: 6	Other _____	Other (specify) _____

PTO-1590 (1-2000)

41265 Access DB# PFE

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Iesha Fields Examiner #: 77985 Date: 4-30-01
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Title of Invention: Malaria Polypeptides

Inventors (please provide full names): (1) Wahlgren, Mats (2) Barragan, Antonio (3) Carlson, Johan (4) Qijun, Chen (5) Fernandez, Victor

Earliest Priority Filing Date: 09/18/98

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please Search Claims
13-17
21-24 & 27
Inventors Patents & Publications

RECEIVED APR 30 2001 (STIC)

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Online Time: 38	Other		Other (specify)	

PTO-1590 (1-2000)

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Entrez Nucleotide

☐ 1: AF003473 **Plasmodium falciparum erythrocyte membrane protein 1 (FCR3S1.2-var1) mRNA, complete cds**

PubMed, Protein, Related Sequences, Taxonomy

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DEFINITION  Plasmodium falciparum erythrocyte membrane protein 1
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ACCESSION   AF003473
VERSION     AF003473.1  GI:2961467
KEYWORDS    .
SOURCE      malaria parasite P. falciparum.
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  AUTHORS   Chen,Q., Barragan,A., Fernandez,V., Sundstrom,A., Schlichtherle,M.,
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  TITLE     Identification of Plasmodium falciparum erythrocyte membrane
            protein 1 (PfEMP1) as the rosetting ligand of the malaria parasite
            P. falciparum
  JOURNAL   J. Exp. Med. 187 (1), 15-23 (1998)
  MEDLINE   98080592
REFERENCE   2  (bases 1 to 6687)
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  TITLE     Direct Submission
  JOURNAL   Submitted (09-MAY-1997) Microbiology and Tumor Biology Center,
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 21/7/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.

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independent host receptors.
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Microbiology and Tumor Biology Center, Karolinska Institutet, The Swedish Institute for Infectious Disease Control, S-171 77 Stockholm, Sweden.

Journal of experimental medicine (UNITED STATES) Jul 3 2000, 192 (1) p1-10, ISSN 0022-1007 Journal Code: I2V

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Erythrocytes infected with mature forms of Plasmodium falciparum do not circulate but are withdrawn from the peripheral circulation; they are bound to the endothelial lining and to uninfected erythrocytes in the microvasculature. Blockage of the blood flow, hampered oxygen delivery, and severe malaria may follow if binding is excessive. The NH(2)-terminal head structure (Duffy binding-like domain 1 [DBL1alpha]-cysteine-rich interdomain region [CIDR1alpha]) of a single species of P. falciparum erythrocyte membrane protein 1 (PfEMP1) is here shown to mediate adherence to multiple host receptors including platelet-endothelial cell adhesion molecule 1 (PECAM-1)/CD31, the blood group A antigen, normal nonimmune immunoglobulin M, three virulence-associated receptor proteins, a heparan sulfate-like glucosaminoglycan, and CD36. DBL2delta was found to mediate additional binding to PECAM-1/CD31. The exceptional binding activity of the PfEMP1 head structure and its relatively conserved nature argues that it holds an important role in erythrocyte sequestration and therefore in the virulence of the malaria parasite.

21/7/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10473678 20344708

Molecular aspects of severe malaria.

Chen Q; Schlichtherle M; Wahlgren M

Microbiology and Tumour Biology Centre, Karolinska Institutet, and Swedish Institute for Infectious Disease Control, S-171 77 Stockholm, Sweden.

Clinical microbiology reviews (UNITED STATES) Jul 2000, 13 (3) p439-50, ISSN 0893-8512 Journal Code: CMR

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

Human infections with Plasmodium falciparum may result in severe forms of malaria. The widespread and rapid development of drug resistance in P. falciparum and the resistance of the disease-transmitting mosquitoes to insecticides make it urgent to understand the molecular background of the pathogenesis of malaria to enable the development of novel approaches to combat the disease. This review focuses on the molecular mechanisms of severe malaria caused by the P. falciparum parasite. The nature of severe malaria and the deleterious effects of parasite-derived toxins and host-induced cytokines are introduced. Sequestration, brought about by cytoadherence and rosetting, is linked to severe malaria and is mediated by multiple receptors on the endothelium and red blood cells. P. falciparum erythrocyte membrane protein 1 (PfEMP1) is the ligand responsible for a majority of binding interactions, and the multiply adhesive features of this sticky molecule are presented. Antigenic variation is also a major feature of PfEMP1 and of the surface of the P. falciparum-infected erythrocyte. Possible mechanisms of P. falciparum antigenic variation in asexual stages are further discussed. We conclude this review with a perspective and suggestions of important aspects for future investigations. (132 Refs.)

21/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10429202 20287404
The duffy-binding-like domain 1 of Plasmodium falciparum erythrocyte membrane protein 1 (PfEMP1) is a heparan sulfate ligand that requires 12 mers for binding.
Barragan A ; Fernandez V ; Chen Q; von Euler A; Wahlgren M ; Spillmann D
Microbiology and Tumor Biology Center, Karolinska Institutet and Swedish Institute for Infectious Disease Control, Stockholm, Sweden.
Blood (UNITED STATES) Jun 1 2000, 95 (11) p3594-9, ISSN 0006-4971 Journal Code: A8G
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The Plasmodium falciparum erythrocyte membrane protein 1 (PfEMP1), present on the surfaces of parasitized red blood cells (pRBC), mediates rosetting, a virulent phenotype. Here, we show that pRBC specifically bind heparan sulfate (HS) and heparin onto their surfaces and that the rosetting ligand PfEMP1 specifically adheres to heparin-Sepharose when extracted from the surfaces of radioiodinated infected RBC. An analysis of the binding properties of the different regions of PfEMP1 provides evidence that the Duffy-binding-like domain-1 (DBL-1) is the predominant ligand involved in HS and heparin binding. Soluble DBL-1 requires a minimal heparin fragment size of a 12-mer (approximately 4 kd) for binding and is critically dependent on N-sulfation. A 12-mer is also the minimal heparin fragment that disrupts naturally formed rosettes. DBL-1 binds specifically to erythrocytes and also to HS from endothelial cells and human aorta but not to chondroitin sulfate A, suggesting that different PfEMP1s mediate adhesion to distinct glycosaminoglycans in individual malaria parasites. Present data suggest that HS on endothelial cells may also be involved in the sequestration of pRBC. Elucidation of these binding mechanisms opens up new possibilities for therapeutic strategies targeting adhesive interactions of pRBC.

21/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10218501 20070972
Rouleaux-forming serum proteins are involved in the rosetting of Plasmodium falciparum-infected erythrocytes.
Treutiger CJ; Scholander C; Carlson J ; McAdam KP; Raynes JG; Falksveden L; Wahlgren M
Microbiology and Tumor Biology Center (MTC), Karolinska Institutet, Stockholm, Sweden. S-171 77.
Experimental parasitology (UNITED STATES) Dec 1999, 93 (4) p215-24, ISSN 0014-4894 Journal Code: EQP
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Excessive sequestration of Plasmodium falciparum-infected (pRBC) and uninfected erythrocytes (RBC) in the microvasculature, cytoadherence, and rosetting, have been suggested to be correlated with the development of

cerebral malaria . P. falciparum erythrocyte membrane protein -1 (PfEMP1) is the parasite-derived adhesin which mediates rosetting. Herein we show that serum proteins are crucial for the rosette formation of four strains of parasites (FCR3S1, TM284, TM180, and R29), whereas the rosettes of a fifth strain (DD2) are serum independent. Some parasites, e.g., FCR3S1, can be depleted of all rosettes by washes in heparin and Na citrate and none of the rosettes remain when the parasite is grown in foetal calf serum or ALBUMAX. Rosettes of other parasites are less sensitive; e.g., 20% of TM180 and R29 and 70% of TM284 rosettes still prevail after cultivation. A serum fraction generated by ion-exchange chromatography and poly-ethylene-glycol precipitation restored 50% of FCR3S1 and approx 40 to 100% of TM180 rosettes. In FCR3S1, antibodies to fibrinogen reverted the effect of the serum fraction and stained fibrinogen bound to the pRBC surface in transmission electron microscopy. Normal, nonimmune IgM and/or IgG was also found attached to the pRBC of the four serum-dependent strains as seen by surface immunofluorescens. Our results suggest that serum proteins, known to participate in rouleaux formation of normal erythrocytes, produce stable rosettes in conjunction with the recently identified parasite-derived rosetting ligand PfEMP1.

21/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10200425 20029800
Small, clonally variant antigens expressed on the surface of the Plasmodium falciparum-infected erythrocyte are encoded by the rif gene family and are the target of human immune responses.
Fernandez V ; Hommel M; Chen Q; Hagblom P; Wahlgren M
Microbiology and Tumor Biology Center, Karolinska Institutet, and the Swedish Institute for Infectious Disease Control, S-17177 Stockholm, Sweden.
Journal of experimental medicine (UNITED STATES) Nov 15 1999, 190 (10) p1393-404, ISSN 0022-1007 Journal Code: I2V
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Disease severity in Plasmodium falciparum infections is a direct consequence of the parasite's efficient evasion of the defense mechanisms of the human host. To date, one parasite-derived molecule, the antigenically variant adhesin P. falciparum erythrocyte membrane protein 1 (PfEMP1), is known to be transported to the infected erythrocyte (pRBC) surface, where it mediates binding to different host receptors. Here we report that multiple additional proteins are expressed by the parasite at the pRBC surface, including a large cluster of clonally variant antigens of 30-45 kD. We have found these antigens to be identical to the rifins, predicted polypeptides encoded by the rif multigene family. These parasite products, formerly called rosettins after their identification in rosetting parasites, are prominently expressed by fresh isolates of P. falciparum. Rifins are immunogenic in natural infections and strain-specifically recognized by human immune sera in immunoprecipitation of surface-labeled pRBC extracts. Furthermore, human immune sera agglutinate pRBCs digested with trypsin at conditions such that radioiodinated PfEMP1 polypeptides are not detected but rifins are detected, suggesting the presence of epitopes in rifins targeted by agglutinating antibodies. When analyzed by two-dimensional electrophoresis,

the rifins resolved into several isoforms in the pI range of 5.5-6.5, indicating molecular microheterogeneity, an additional potential novel source of antigenic diversity in P. falciparum. Prominent polypeptides of 20, 22, 76-80, 140, and 170 kD were also detected on the surfaces of pRBCs bearing in vitro-propagated or field-isolated parasites. In this report, we describe the rifins, the second family of clonally variant antigens known to be displayed by P. falciparum on the surface of the infected erythrocyte.

21/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09855460 99189744
Waves of malarial var-iations.
Wahlgren M ; Fernandez V ; Chen Q; Svard S; Hagblom P
Microbiology and Tumor Biology Center, Karolinska Institutet, Stockholm, Sweden. mats.wahlgren@smi.ki.se
Cell (UNITED STATES) Mar 5 1999, 96 (5) p603-6, ISSN 0092-8674
Journal Code: CQ4
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
(15 Refs.)

21/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09571421 98352787
Developmental selection of var gene expression in Plasmodium falciparum.
Chen Q; Fernandez V ; Sundstrom A; Schlichtherle M; Datta S; Hagblom P; Wahlgren M
Microbiology and Tumor Biology Center, Karolinska Institutet, Stockholm, Sweden.
Nature (ENGLAND) Jul 23 1998, 394 (6691) p392-5, ISSN 0028-0836
Journal Code: NSC
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The protozoan Plasmodium falciparum causes lethal malaria. Adhesion of erythrocytes infected with P. falciparum to vascular endothelium and to uninfected red blood cells (rosetting) may be involved in the pathogenesis of severe malaria. The binding is mediated by the antigenically variant erythrocyte-membrane-protein-1 (PfEMP-1), which is encoded by members of the P. falciparum var gene family. The control of expression and switching of var genes seems to lack resemblance to mechanisms operating in variant gene families of other microbial pathogens. Here we show that multiple, distinct var gene transcripts (about 24 or more) can be detected by reverse transcription and polymerase chain reaction in bulk cultures of the rosetting parasite FCR3S1.2, despite the adhesive homogeneity of the cultures. We also detected several var transcripts in single erythrocytes infected with a ring-stage parasite of FCR3S1.2, and found that different var genes are transcribed simultaneously from several chromosomes in the same cell. In contrast, we detected only one var transcript, FCR3S1.2 var-1, which encodes the rosetting PfEMP-1 protein, in individual rosette-adhesive trophozoite-infected cells, and we found only one PfEMP-1

type at the erythrocyte surface by labelling with 125iodine and immunoprecipitation. We conclude that a single P. falciparum parasite simultaneously transcribes multiple var genes but, through a developmentally regulated process, selects only one PfEMP-1 to reach the surface of the host cell.

21/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09520893 98261553
Multiple adhesive phenotypes linked to rosetting binding of erythrocytes in Plasmodium falciparum malaria.
Fernandez V ; Treutiger CJ; Nash GB; Wahlgren M
Microbiology and Tumor Biology Center, Karolinska Institutet, and Swedish Institute for Infectious Disease Control, S-171 77 Stockholm, Sweden.
Infection and immunity (UNITED STATES) Jun 1998, 66 (6) p2969-75, ISSN 0019-9567 Journal Code: GO7
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The cerebral form of severe malaria is associated with excessive intravascular sequestration of Plasmodium falciparum-infected erythrocytes (PRBC). Retention and accumulation of PRBC may lead to occlusion of brain microvessels and direct the triggering of acute pathologic changes. Here we report that by selection, cloning, and subcloning, we have identified rare P. falciparum parasites expressing a pan-adhesive phenotype linked to erythrocyte rosetting, a previously identified correlate of cerebral malaria. Rosetting PRBC not only bound uninfected erythrocytes but also formed autoagglutinates, adhered to endothelial cells, and bound to CD36, immunoglobulins, and the blood group A antigen. The linkage of rosetting, autoagglutination, and cytoadherence involved the coexpression on a single PRBC of ligands with multiple specificities and the binding to two or more receptors on erythrocytes and to at least two other cell adhesion molecules, including a new endothelial cell receptor for P. falciparum-infected erythrocytes. Limited proteolysis that differentially cleaved the rosetting ligand PfEMP1 from the PRBC surface abrogated all the binding phenotypes of these parasites, implicating the variant antigen PfEMP1 as a carrier of multiple ligand specificities. The results encourage the further study of pan-adhesion as a potentially important parasite phenotype in the pathogenesis of severe P. falciparum malaria.

21/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09369367 98080592
Identification of Plasmodium falciparum erythrocyte membrane protein 1 (PfEMP1) as the rosetting ligand of the malaria parasite P. falciparum.
Chen Q; Barragan A ; Fernandez V ; Sundstrom A; Schlichtherle M; Sahlen A; Carlson J ; Datta S; Wahlgren M
Microbiology and Tumor Biology Center, Karolinska Institutet, the Swedish Institute for Infectious Disease Control, S-171 77 Stockholm, Sweden.
Journal of experimental medicine (UNITED STATES) Jan 5 1998, 187 (1) p15-23, ISSN 0022-1007 Journal Code: I2V

Languages: ENGLISH
Document type: JOURNAL ARTICLE
Severe Plasmodium falciparum malaria is characterized by excessive sequestration of infected and uninfected erythrocytes in the microvasculature of the affected organ. Rosetting, the adhesion of P. falciparum-infected erythrocytes to uninfected erythrocytes is a virulent parasite phenotype associated with the occurrence of severe malaria. Here we report on the identification by single-cell reverse transcriptase PCR and cDNA cloning of the adhesive ligand P. falciparum erythrocyte membrane protein 1 (PfEMP1). Rosetting PfEMP1 contains clusters of glycosaminoglycan-binding motifs. A recombinant fusion protein (Duffy binding-like 1-glutathione S transferase; Duffy binding-like-1-GST) was found to adhere directly to normal erythrocytes, disrupt naturally formed rosettes, block rosette reformation, and bind to a heparin-Sepharose matrix. The adhesive interactions could be inhibited with heparan sulfate or enzymes that remove heparan sulfate from the cell surface whereas other enzymes or similar glycosaminoglycans of a like negative charge did not affect the binding. PfEMP1 is suggested to be the rosetting ligand and heparan sulfate, or a heparan sulfate-like molecule, the receptor both for PfEMP1 binding and naturally formed erythrocyte rosettes.

21/7/10 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12079605 BIOSIS NO.: 199900374454
Cell-to-cell interactions of importance for the development of severe Plasmodium falciparum malaria.
AUTHOR: Wahlgren Mats (a
AUTHOR ADDRESS: (a)Microbiology and Tumor Biology Centre, Karolinska Institutet, Stockholm**Sweden
JOURNAL: Biochemical Society Transactions 27 (3):pA85 1999
CONFERENCE/MEETING: 668th Meeting of the Biochemical Society Glasgow, Scotland, UK April 7-9, 1999
SPONSOR: Biochemical Society
ISSN: 0300-5127
RECORD TYPE: Citation
LANGUAGE: English

21/7/11 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11327337 BIOSIS NO.: 199800108669
The molecular pathogenesis of severe malaria.
AUTHOR: Wahlgren Mats (a
AUTHOR ADDRESS: (a)Microbiol. Tumor Biol. Center, Karolinska Inst., Box 280, S-171 77 Stockholm**Sweden
JOURNAL: Memorias do Instituto Oswaldo Cruz 92 (SUPPL. 1):p25-26 Nov., 1997
CONFERENCE/MEETING: XIII Meeting of the Brazilian Society of Protozoology and the XXIV Annual Meeting on Basic Research in Chagas' Disease Caxambu, Brazil November 11-14, 1997
SPONSOR: Brazilian Society of Protozoology
ISSN: 0074-0276

RECORD TYPE: Citation
LANGUAGE: English

21/7/12 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

130251214 CA: 130(19)251214v PATENT
Malaria polypeptides
INVENTOR(AUTHOR): Wahlgren, Mats; Barragan, Antonio; Carlson, Johan; Qijun, Chen; Fernandez, Victor
LOCATION: Swed.
ASSIGNEE: Karolinska Innovations AB
PATENT: PCT International ; WO 9915557 A1 DATE: 19990401
APPLICATION: WO 98SE1675 (19980918) *SE 973386 (19970919)
PAGES: 80 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-014/445A; A61K-038/17B DESIGNATED COUNTRIES: AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; GM; HR; HU; ID; IL; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH ; GM; KE; LS; MW; SD; SZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG
SECTION:
CA215002 Immunochemistry
IDENTIFIERS: Plasmodium falciparum erythrocyte membrane protein 1, PfEMP1 ligand carbohydrate receptor malaria vaccine
DESCRIPTORS:
Receptors...
carbohydrate; identification and prepn. of Plasmodium falciparum erythrocyte membrane protein-1 for vaccination and carbohydrate receptor contg. glucosaminoglycan moiety
Antibodies... Drug carriers(drug delivery systems)...
Glycosaminoglycans,biological studies... Ligands... Malaria... Molecular cloning... Plasmodium falciparum... Protein sequences... Sulfated glycosaminoglycans... Vaccines...
identification and prepn. of Plasmodium falciparum erythrocyte membrane protein-1 for vaccination and carbohydrate receptor contg. glucosaminoglycan moiety
Membrane proteins...
PfEMP1 (Plasmodium falciparum erythrocyte membrane protein 1); identification and prepn. of Plasmodium falciparum erythrocyte membrane protein-1 for vaccination and carbohydrate receptor contg. glucos
Carbohydrates,biological studies...
receptor; identification and prepn. of Plasmodium falciparum erythrocyte membrane protein-1 for vaccination and carbohydrate receptor contg. glucosaminoglycan moiety
Proteins(specific proteins and subclasses)...
280,000-300,000 mol. wt.; identification and prepn. of Plasmodium falciparum erythrocyte membrane protein-1 for vaccination and carbohydrate receptor contg. glucosaminoglycan moiety
CAS REGISTRY NUMBERS:
202877-46-1 amino acid sequence; identification and prepn. of Plasmodium falciparum erythrocyte membrane protein-1 for vaccination and carbohydrate receptor contg. glucosaminoglycan moiety

9005-49-6 biological studies, identification and prepn. of Plasmodium falciparum erythrocyte membrane protein-1 for vaccination and carbohydrate receptor contg. glucosaminoglycan moiety
9072-19-9 identification and prepn. of Plasmodium falciparum erythrocyte membrane protein-1 for vaccination and carbohydrate receptor contg. glucosaminoglycan moiety

21/7/13 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

105170174 CA: 105(19)170174p CONFERENCE PROCEEDING
Specificity and inhibitory activity of antibodies to a Plasmodium falciparum antigen (Pf 155) and its major amino acid repeat sequence
AUTHOR(S): Perlmann, Peter; Berzins, Klavs; Carlsson, Jan; Perlmann, Hedvig; Sjoeberg, Katarina; Troye-Blomberg, Marita; Udomsangpetch, Rachanee ; Wahlgren, Mats; Waahlin, Birgitta; et al.
LOCATION: Dep. Immunol., Univ. Stockholm, S-106 91, Stockholm, Swed.
JOURNAL: Vaccines 86, New Approaches Immun., (Proc. Conf.) EDITOR: Brown, Fred (Ed), Chanock, Robert M. (Ed), Lerner, Richard Alan (Ed),
DATE: 1986 PAGES: 149-55 CODEN: 55ENAN LANGUAGE: English
MEETING DATE: 850000 PUBLISHER: Cold Spring Harbor Lab.,Cold Spring Harbor, N. Y
SECTION:
CA115002 Immunochemistry
IDENTIFIERS: Plasmodium antigen Pf155 erythrocyte
DESCRIPTORS:
Plasmodium falciparum...
antigen Pf155 of, in infected erythrocyte membrane of human, characterization of
Glycophorins...
antigen Pf155 of Plasmodium falciparum binding to, of human erythrocyte
Proteins,Pf 155...
of Plasmodium falciparum, in infected erythrocyte membrane of human, characterization of
Erythrocyte...
Plasmodium falciparum infestation of human, antigen Pf 155 in
Antibodies,monoclonal...
to Plasmodium falciparum antigen Pf 155, human erythrocyte invasion by merozoites inhibition by

21/7/14 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

99210689 CA: 99(25)210689b JOURNAL
A comparison of knobby (K+) and knobless (K-) parasites from two strains of Plasmodium falciparum
AUTHOR(S): Hadley, Terence J.; Leech, James H.; Green, Theodore J.; Daniel, Wendell A.; Wahlgren, Mats; Miller, Louis H.; Howard, Russell J.
LOCATION: Lab. Parasit. Dis., Natl. Inst. Allergy Infect. Dis., Bethesda, MD, 20205, USA
JOURNAL: Mol. Biochem. Parasitol. DATE: 1983 VOLUME: 9 NUMBER: 3
PAGES: 271-8 CODEN: MBIPDP ISSN: 0166-6851 LANGUAGE: English
SECTION:

CA114003 Mammalian Pathological Biochemistry
CA110XXX Microbial Biochemistry
  IDENTIFIERS: Plasmodium infection erythrocyte knob protein
  DESCRIPTORS:
Plasmodium falciparum...
    histidine-labeled protein of knob-pos. and knob-neg. strains of, erythrocyte knob protein in relation to
Proteins...
    of Plasmodium falciparum knob-pos. and knob-neg. strains, erythrocyte knob protein in relation to
Erythrocyte...
    protein of cell membrane knob of, protein of Plasmodium falciparum knob-pos. and knob-neg. strains in relation to
Cell membrane...
    protein of knob of erythrocyte, protein of Plasmodium falciparum knob-pos. and knob-neg. strains in relation to

21/7/15 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

012448584
WPI Acc No: 1999-254692/199921
New isolated malaria polypeptides
Patent Assignee: KAROLINSKA INNOVATIONS AB (KARO-N)
Inventor: BARRAGAN A ; CARLSON J ; FERNANDEZ V ; QIJUN C ; WAHLGREN M
Number of Countries: 083 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9915557	A1	19990401	WO 98SE1675	A	19980918	199921	B
AU 9892884	A	19990412	AU 9892884	A	19980918	199934	
EP 1015483	A1	20000705	EP 98945703	A	19980918	200035	
			WO 98SE1675	A	19980918		

Priority Applications (No Type Date): SE 973386 A 19970919
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9915557	A1	E	79	C07K-014/445	

   Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
   Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

AU 9892884	A		C07K-014/445	Based on patent WO 9915557
EP 1015483	A1	E	C07K-014/445	Based on patent WO 9915557

   Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

Abstract (Basic): WO 9915557 A1
        NOVELTY - Novel carbohydrates and novel malaria erythrocyte membrane proteins to which they bind are disclosed.
        DETAILED DESCRIPTION - A carbohydrate which exhibits at least one negatively charged glycosamino-glycan (GAG)-like moiety, and which is capable of specific binding to a malaria erythrocyte membrane protein (MEMP) or a functional analog is new.

INDEPENDENT CLAIMS are also included for:

(1) an isolated polypeptide originating from a MEMP comprising an amino-terminal part of a sequence (I) (2228 amino acids in length) or an analog;

(2) a polypeptide originating from a MEMP comprising at least about 300 amino acids of sequence (I) or a functional analog;

(3) a nucleic acid encoding a polypeptide as in (1) or (2);

(4) a nucleic acid capable of specific hybridization under stringent conditions to a nucleic acid as in (3);

(5) an antibody which is specifically immunoreactive with a polypeptide as in (1) or (2) or with an analog.

ACTIVITY - Antiaggregational; Antiocclusion, Binding inhibitory; Antimalarial.

MECHANISM OF ACTION - The carbohydrates are capable of acting as receptors for malaria antigens present on the surfaces of malaria infected erythrocytes, by binding to these antigens the carbohydrates prevent rosette formation by the blood cells, this prevents occlusion of capillaries as is seen in cerebral malaria caused by Plasmodium falciparum.

USE - The carbohydrates can be used to treat a patient suffering from malaria especially caused by Plasmodium falciparum (claimed). The polypeptides can also be used to treat malaria or to vaccinate against it , especially malaria caused by Plasmodium falciparum(claimed) . The polypeptides can also be used as a model to identify compounds that bind to MEMP (claimed). The antibody can also be used to treat or prevent a malaria, especially caused by Plasmodium falciparum(claimed). The carbohydrates, polypeptides and antibodies can be used as a medicament for dissolving the rosettes formed by erythrocytes infected by a malaria parasite. They are effective in dissolving and preventing the occlusion of blood vessels, especially in cerebral malaria. They can also be used for the design of agents for treating malaria. The products can also be used for detection, diagnosis and drug screening.

pp; 79 DwgNo 0/4

Derwent Class: B04; C06; D16

International Patent Class (Main): C07K-014/445

International Patent Class (Additional): A61K-038/17

?t 28/7/all

28/7/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10100914 98206748

Non-detergent sulphobetaines enhance the recovery of membrane and/or cytoskeleton-associated proteins and active proteases from erythrocytes infected by Plasmodium falciparum.

Blisnick T; Morales-Betoulle ME; Vuillard L; Rabilloud T; Braun Breton C

Unit of Experimental Parasitology, Institut Pasteur, Paris, France.

European journal of biochemistry (GERMANY) Mar 15 1998, 252 (3) p537 41, ISSN 0014 2956 Journal Code: EMZ

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A better understanding of the causative agent's biology and the definition of new targets for the development of drugs and/or specific immune responses is necessary to face the spred of drug-resistant malaria in developing countries and the absence of an efficient vaccine against this most important infectious disease. Non-detergent sulphobetaines

enhance the recovery and isoelectric focussing of active Plasmodium falciparum proteases, cytoskeleton-associated proteins and Maurer's cleft-associated proteins. This is a significant advantage for the purification of such proteins and might help pinpoint their role for red blood cell rupture and merozoite release.

28/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09522489 98226171
Identification of peripheral membrane proteins associated with the tubo-vesicular network of Plasmodium falciparum infected erythrocytes.
Martinez SL; Clavijo CA; Winograd E
Laboratorio de Biologia Celular, Instituto Nacional de Salud, Bogota, Colombia.
Molecular and biochemical parasitology (NETHERLANDS) Mar 15 1998, 91 (2) p273-80, ISSN 0166-6851 Journal Code: NOR
Languages: ENGLISH
Document type: JOURNAL ARTICLE
During intracellular development of the malarial parasite numerous membranous vesicles appear in the infected erythrocyte cytoplasm between the parasitophorous vacuolar membrane (PVM) and the erythrocyte plasma membrane. In this study we describe the characterization of a monoclonal antibody which recognizes two major parasite-encoded proteins of 50 and 41 kDa. Immunofluorescence and immunoelectron microscopy demonstrated that the monoclonal antibody reacts with cytoplasmic vesicles of Plasmodium falciparum infected erythrocyte referred to as Maurer's clefts. The antigens recognized by the monoclonal antibody were expressed very early during the erythrocytic life cycle of the parasite, and remained tightly associated within membrane vesicles even after merozoites are released from infected erythrocytes. The antigens were partially soluble in non-ionic detergents, and were released from the membrane by alkali treatment , indicating that the proteins recognized by the monoclonal antibody are peripheral membrane proteins. It is proposed that the 50 and 41 kDa antigens might be part of an underlying membrane skeletal network that provides structural support to vesicles and tubules present in the infected erythrocyte cytoplasm.

28/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09433187 98160250
Parasite antigens on the infected red cell surface are targets for naturally acquired immunity to malaria.
Bull PC; Lowe BS; Kortok M; Molyneux CS; Newbold CI; Marsh K
Kenya Medical Research Institute CRC, Kilifi Unit. pbull@africaonline.co.ke
Nature medicine (UNITED STATES) Mar 1998, 4 (3) p358-60, ISSN 1078-8956 Journal Code: CG5
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The feasibility of a malaria vaccine is supported by the fact that children in endemic areas develop naturally acquired immunity to disease.

Development of disease immunity is characterized by a decrease in the frequency and severity of disease episodes over several years despite almost continuous infection, suggesting that immunity may develop through the acquisition of a repertoire of specific, protective antibodies directed against polymorphic target antigens. Plasmodium falciparum erythrocyte membrane protein 1 (PfEMP1) is a potentially important family of target antigens, because these proteins are inserted into the red cell surface and are prominently exposed and because they are highly polymorphic and undergo clonal antigenic variation, a mechanism of immune evasion maintained by a large family of var genes. In a large prospective study of Kenyan children, we have used the fact that anti-PfEMP1 antibodies agglutinate infected erythrocytes in a variant-specific manner, to show that the PfEMP1 variants expressed during episodes of clinical malaria were less likely to be recognized by the corresponding child's own preexisting antibody response than by that of children of the same age from the same community. In contrast, a heterologous parasite isolate was just as likely to be recognized. The apparent selective pressure exerted by established anti-PfEMP1 antibodies on infecting parasites supports the idea that such responses provide variant-specific protection against disease.

28/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09289289 98008145
Identification of a region of PfEMP1 that mediates adherence of Plasmodium falciparum infected erythrocytes to CD36: conserved function with variant sequence.
Baruch DI; Ma XC; Singh HB; Bi X; Pasloske BL; Howard RJ
Affymax Research Institute, Santa Clara, CA, USA.
Blood (UNITED STATES) Nov 1 1997, 90 (9) p3766-75, ISSN 0006-4971
Journal Code: A8G
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Adherence of mature parasitized erythrocytes (PE) of Plasmodium falciparum to microvascular endothelial cells contributes directly to the virulence and pathology of this human malaria . The malarial variant antigen, P falciparum erythrocyte membrane protein 1 (PfEMP1), has been implicated as the PE receptor for CD36 on endothelial cells. We identified the region of PfEMP1 that mediates adherence of PE to CD36 and showed that a recombinant protein fragment from this region blocked and reversed adherence of antigenically different parasites. Sequence variation was evident in the CD36 binding domain of different PfEMP1 genes, yet many highly conserved residues, particularly cysteine residues, are evident. This suggests a highly conserved shape that mediates adherence to CD36. Immunization with the CD36-binding domain elicited sera that are cross-reactive with the different recombinant proteins but are strain-specific for the PE surface. Novel anti-adherence therapeutics and a malaria vaccine may derived from exploitation of the structure of the CD36 binding domain of PfEMP1.

28/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09242887 97437019
Knob proteins in falciparum malaria.
Sharma YD
Department of Biotechnology, All India Institute of Medical Sciences, New Delhi.
Indian journal of medical research (INDIA) Aug 1997, 106 p53-62, ISSN 0971-5916 Journal Code: GJF
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Knob proteins play a significant role in the pathophysiology of cerebral malaria caused by Plasmodium falciparum. Most of these proteins are of parasite origin and can be divided into two major classes: (i) the cytoadherent proteins present at the surface of the knobs; and (ii) the submembranous structural proteins which are placed towards the cytoplasmic side in the knobs. Several surface proteins [viz., P. falciparum -infected erythrocyte membrane protein -1 (PFEMP-1), sequestrin, pfalhesin] and submembranous structural proteins [viz., knob-associated histidine-rich protein (KAHRP), PFEMP-2, PFEMP-3] of the knobs have been identified and characterized to a certain extent. The structural proteins interact with several host (e.g., spectrin, actin, band 4.1 etc.) as well as parasite (e.g., PFEMP-1) molecules to produce functional knobs. The surface proteins on the other hand interact with several adhesion molecules of the endothelial cell through receptor-ligand type of binding. Knob proteins are important from the point of view of malaria control since immunotherapeutic agents can be developed to block as well as reverse the cytoadherence phenomenon. The surface proteins are also good vaccine candidates except that they show a high rate of antigenic variation. Nevertheless, the use of ribozyme or antisense oligonucleotides to inhibit the expression of knob proteins (e.g., KAHRP alone or with surface protein) can be used as a molecular therapeutic agent. (55 Refs.)

28/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09190496 97373957
P. falciparum rosetting mediated by a parasite-variant erythrocyte membrane protein and complement-receptor 1.
Rowe JA; Moulds JM; Newbold CI; Miller LH
Laboratory of Parasitic Diseases, NIAID, NIH, Bethesda, Maryland 20892, USA. arowe@worf.molbiol.ox.ac.uk
Nature (ENGLAND) Jul 17 1997, 388 (6639) p292-5, ISSN 0028-0836 Journal Code: NSC
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The factors determining disease severity in malaria are complex and include host polymorphisms, acquired immunity and parasite virulence. Studies in Africa have shown that severe malaria is associated with the ability of erythrocytes infected with the parasite Plasmodium falciparum to bind uninfected erythrocytes and form rosettes. The molecular basis of resetting is not well understood, although a group of low-molecular-mass proteins called rosettins have been described as potential parasite ligands. Infected erythrocytes also bind to endothelial cells, and this interaction is mediated by the parasite-derived variant erythrocyte membrane protein PfEMP1, which is encoded by the var gene family. Here we report that the parasite ligand for rosetting in a P. falciparum clone is

PfEMP1, encoded by a specific var gene. We also report that complement-receptor 1 (CR1) on erythrocytes plays a role in the formation of rosettes and that erythrocytes with a common African CR1 polymorphism (S1(a-)) have reduced adhesion to the domain of PfEMP1 that binds normal erythrocytes. Thus we describe a new adhesive function for PfEMP1 and raise the possibility that CR1 polymorphisms in Africans that influence the interaction between erythrocytes and PfEMP1 may protect against severe malaria.

28/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09166878 97326106
Defining the minimal domain of the Plasmodium falciparum protein MESA involved in the interaction with the red cell membrane skeletal protein 4.1.
Bennett BJ; Mohandas N; Coppel RL
Walter and Eliza Hall Institute of Medical Research, Victoria 3050, Australia.
Journal of biological chemistry (UNITED STATES) Jun 13 1997, 272 (24) p15299-306, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: DK32094-10, DK, NIDDK
Languages: ENGLISH
Document type: JOURNAL ARTICLE
During part of its life cycle, the protozoan parasite Plasmodium falciparum lives within the human red blood cell and modifies both the structural and functional properties of the red cell. It does this by synthesizing a number of polypeptides that it transports into the red cell cytoplasm and to the red cell membrane. One of these transported proteins, MESA (mature parasite-infected erythrocyte surface antigen), is anchored to the red cell membrane by noncovalent interaction with erythrocyte protein 4.1. We have utilized a combination of in vitro transcription and translation and a membrane binding assay to identify the protein sequence involved in anchoring MESA to the membrane. Labeled fragments of different regions of the MESA protein were evaluated for their ability to bind to inside-out vesicle membrane preparations of human red cells. Binding was dependent on the presence of red cell membrane proteins and was abolished either by trypsin treatment or by selective depletion of membrane proteins. Binding was specific and could be inhibited by the addition of competing protein, with an IC50 of (6.3 +/- 1.2) x 10(-7) M, indicative of a moderate affinity interaction. Fractionation studies demonstrated that binding fragments interacted most efficiently with membrane protein fractions that had been enriched in protein 4.1. Binding inhibition experiments using synthetic peptides identified the binding domain of MESA for protein 4.1 as a 19-residue sequence near the amino terminus of MESA, a region capable of forming an amphipathic helix.

28/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08668637 94178925
Preferential binding of Plasmodium falciparum SERA and rhoptry proteins to erythrocyte membrane inner leaflet phospholipids.

Perkins ME; Ziefer A
Laboratory of Biochemical Parasitology, Rockefeller University, New York, New York 10023.
Infection and immunity (UNITED STATES) Apr 1994, 62 (4) p1207-12, ISSN 0019-9567 Journal Code: GO7
Contract/Grant No.: AI 19585, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Proteins of an apical organelle, the rhoptry, of Plasmodium falciparum are secreted into the host erythrocyte membrane during merozoite invasion. To identify the membrane-binding site for rhoptry proteins, we examined the binding of parasite proteins to phospholipid vesicles. A specific interaction between the rhoptry proteins of 140, 130, and 110 kDa to vesicles containing phosphatidylserine and phosphatidylinositol was observed. Both phospholipids are preferentially localized on the inner leaflet of the bilayer. Binding to other phospholipids, including sphingomyelin, was considerably less. In addition, the 120-kDa serine repeat antigen known as SERA, which was determined to be present on the merozoite, bound to phosphatidylserine vesicles and much less to vesicles of other phospholipids. Both the rhoptry and SERA proteins exhibited a preference for phosphatidylserine with short acyl side chains. Specific binding of SERA and the rhoptry proteins to phospholipids of the inner leaflet of membranes suggests a possible mechanism by which the protein facilitate invasion into host cells.

28/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08585193 96018774
Plasmodium falciparum: effects of membrane modulating agents on direct binding of rhoptry proteins to human erythrocytes.
Ndengele MM; Messineo DG; Sam-Yellowe T; Harwalkar JA
Department of Biology, Cleveland State University, Ohio 44115, USA.
Experimental parasitology (UNITED STATES) Sep 1995, 81 (2) p191-201, ISSN 0014-4894 Journal Code: EQP
Languages: ENGLISH
Document type: JOURNAL ARTICLE

We studied the effects of membrane modulation on the interaction of Plasmodium falciparum rhoptry proteins of 140/130/110 kDa (Rhop-H) with human and mouse erythrocytes. Cells treated with 2-(2-methoxyethoxy)ethyl-8-(cis-2-n-octylcyclopropyl)octanoate, myristoleyl alcohol, and proteins extracted with sublytic concentrations of membrane solubilizing detergents were used in erythrocyte binding assays . Protein binding was evaluated by immunoblotting using Rhop-H- and SERA-specific antisera, 1B9, K15, and 5E3, respectively. Protein binding to liposomes prepared with dipalmitoyl-L-alpha-phosphatidylcholine (DPPC) or dilauroyl-L-alpha-phosphatidylcholine (DLPC) was also examined. Our results show that erythrocyte membrane modulation markedly enhanced direct Rhop-H binding to intact human erythrocytes. Binding of SERA to intact human erythrocytes appeared unaffected. Both DPPC and DLPC liposomes had similar Rhop-H and SERA protein binding activities. However, binding to DLPC liposomes was reduced. Rhop-H and SERA extracted with the detergents octanoyl-N-methylglucamide, decanoyl-N-methylglucamide, sodium deoxycholate , and 3-[(3-cholamidopropyl)dimethylammonio]-1-propane sulfonate bound directly to intact human erythrocytes, probably by partitioning

hydrophobically into the membranes. Sodium carbonate treatment demonstrated a nonintegral association of Rhop-H with the erythrocyte membrane during invasion. Membrane modulation may expose cryptic phospholipid binding sites in the bilayer.

28/7/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08578767 95330812
Cloning the P. falciparum gene encoding PfEMP1, a malarial variant antigen and adherence receptor on the surface of parasitized human erythrocytes [see comments]
Baruch DI; Pasloske BL; Singh HB; Bi X; Ma XC; Feldman M; Taraschi TF; Howard RJ
Affymax Research Institute Santa Clara, California 95051, USA.
Cell (UNITED STATES) Jul 14 1995, 82 (1) p77-87, ISSN 0092-8674 Journal Code: CQ4
Contract/Grant No.: AI 27247, AI, NIAID
Comment in Cell 1995 Jul 14;82(1):1-4
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Plasmodium falciparum-infected human erythrocytes evade host immunity by expression of a cell-surface variant antigen and receptors for adherence to endothelial cells. These properties have been ascribed to P. falciparum erythrocyte membrane protein 1 (PfEMP1), an antigenically diverse malarial protein of 200-350 kDa on the surface of parasitized erythrocytes (PEs). We describe the cloning of two related PfEMP1 genes from the Malayan Camp (MC) parasite strain. Antibodies generated against recombinant protein fragments of the genes were specific for MC strain PfEMP1 protein. These antibodies reacted only with the surface of MC strain PEs and blocked adherence of these cells to CD36 but without effect on adherence to thrombospondin. Multiple forms of the PfEMP1 gene are apparent in MC parasites. The molecular basis for antigenic variation in malaria and adherence of infected erythrocytes to host cells can now be pursued.

28/7/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08105269 95140052
A Plasmodium falciparum isolate with a chromosome 9 deletion expresses a trypsin-resistant cytoadherence molecule.
Chaiyaroj SC; Coppel RL; Magowan C; Brown GV
Walter and Eliza Hall Institute of Medical Research, Post Office Royal Melbourne Hospital, Victoria, Australia.
Molecular and biochemical parasitology (NETHERLANDS) Sep 1994, 67 (1) p21-30, ISSN 0166-6851 Journal Code: MOR
Contract/Grant No.: DK 32094-10, DK, NIDDK
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Sequestration of Plasmodium falciparum infected erythrocytes in the cerebral circulation is strongly implicated in the pathogenesis of cerebral malaria. From previous studies it was postulated that genes essential for cytoadherence were located on the right arm of chromosome 9 as P.

falciparum isolates with a deletion in this region lost the capacity to cytoadhere in vitro and no longer expressed Plasmodium falciparum erythrocyte membrane protein -1 (PfEMP-1) on the surface of the infected cells. We have selected a P. falciparum isolate from Papua New Guinea for high levels of cytoadherence to human umbilical vein endothelial cells (HUVECs) and have shown that the cloned parasite has several novel properties related to cytoadherence. The cloned parasite adheres to HUVECs, does not bind to melanoma cells, and expresses a surface molecule with most of the properties of PfEMP-1, despite a deletion in the right arm of chromosome 9. Interestingly, the surface expressed PfEMP-1 in this strain is resistant to trypsin treatment and infected cells continue to cytoadhere after trypsin digestion at a concentration of 100 micrograms ml-1. The receptor on HUVECs for the cloned parasite lines is a molecule different from any previously described, as parasitized cells do not adhere to soluble intercellular adhesion molecule 1, thrombospondin, vascular cell adhesion molecule 1, E-selectin or P-selectin, nor to CD36. Our work, taken together with the results from previous studies, suggest that the ability of parasites to cytoadhere is encoded in at least two distinct genomic locations in the parasite, and the diversity of receptor-ligand interaction is greater than previously described.

28/7/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07995263 94359537
Glycophorin B as an EBA-175 independent Plasmodium falciparum receptor of human erythrocytes.

Dolan SA; Proctor JL; Alling DW; Okubo Y; Wellems TE; Miller LH
Laboratory of Malaria Research, National Institute of Allergy and Infectious Diseases, Bethesda, MD 20892.

Molecular and biochemical parasitology (NETHERLANDS) Mar 1994, 64 (1) p55-63, ISSN 0166-6851 Journal Code: NOR
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Invasion of erythrocytes by malaria parasites involves multiple receptor-ligand interactions. To elucidate these pathways, we made use of four parasite clones with differing specificities for invasion, erythrocytes that are mutant for either glycophorin A or B, and enzyme modification of the erythrocyte surface with neuraminidase and trypsin. Neuraminidase alone abolishes invasion of two parasite clones (Dd2, FCR3/A2); these invade after trypsin treatment alone. A third clone (7G8) is unable to invade trypsin-treated erythrocytes. The fourth clone (HB3) can invade after either neuraminidase or trypsin treatment . The receptor for invasion of trypsin-treated erythrocytes was explored in two ways: treatment of trypsin-treated normal cells with neuraminidase, and trypsin treatment of glycophorin B-deficient cells. Both treatments eliminated invasion by all clones, indicating that the trypsin-independent pathway uses sialic acid and glycophorin B. To identify parasite proteins involved in the different pathways, erythrocyte binding assays were performed with soluble parasite proteins from each clone. Based on binding assays using erythrocytes that lack glycophorin A, the parasite protein known as EBA-175 appears to bind predominantly to glycophorin A. In contrast, the glycophorin B pathway does not appear to involve EBA-175, as binding of EBA-175 was similarly reduced to trypsin-treated normal and trypsin-treated glycophorin B-deficient erythrocytes. Thus, the glycophorin

B-dependent, sialic acid-dependent invasion of trypsin-treated normal erythrocytes uses a different parasite ligand, indicating two or more sialic-dependent pathways for invasion. Clone 7G8, which cannot invade trypsin-treated erythrocytes, may be missing the ligand for invasion via glycophorin B.(ABSTRACT TRUNCATED AT 250 WORDS)

28/7/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07980357 94336255
Characterization of membrane proteins exported from Plasmodium falciparum into the host erythrocyte.
Johnson D; Gunther K; Ansorge I; Benting J; Kent A; Bannister L; Ridley R ; Lingelbach K
Department of Molecular Biology, University of Edinburgh, UK.
Parasitology (ENGLAND) Jul 1994, 109 (Pt 1) p1-9, ISSN 0031-1820 Journal Code: ORO
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Plasmodium falciparum is an intracellular parasite of the red blood cell. During development it exports proteins which are transported to specific locations within the host erythrocyte. We have begun to identify and characterize exported membrane proteins of P. falciparum in order to obtain specific marker molecules for the study of the mechanisms involved in the distribution of parasite-derived proteins within the host cell. In this report we describe the characterization of a 35 kDa protein which is recognized by a monoclonal antibody. The protein is tightly associated with membranes isolated from infected erythrocytes; it is resistant to extraction with alkali and soluble after treatment with detergents. It is located at the membrane of the parasitophorous vacuole and in membrane-bound compartments which appear in the cytoplasm of the infected erythrocyte. The protein co-localizes with the previously described exported protein-1 (exp-1). Considering its localization and physical similarities to exp-1, we name the 35 kDa protein the exported protein-2 (exp-2).

28/7/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07739503 94187797
Proteolytic digestion of band 3 at an external site alters the erythrocyte membrane organisation and may facilitate malarial invasion.
McPherson RA; Donald DR; Sawyer WH; Tilley L
Department of Biochemistry, La Trobe University, Bundoora, Victoria, Australia.
Molecular and biochemical parasitology (NETHERLANDS) Dec 1993, 62 (2) p233-42, ISSN 0166-6851 Journal Code: NOR
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Invasion of human erythrocytes by Plasmodium falciparum is inhibited by chymostatin. This suggests that digestion of erythrocyte surface proteins by a protease with chymotrypsin-like activity may be involved in the invasion process. We find that treatment of intact erythrocytes with

chymotrypsin cleaves the integral membrane protein, band 3, generating a major fragment with an apparent molecular weight of 58 kDa. We have used measurements of the rotational mobility of band 3, labelled with the phosphorescence probe, eosin-5-maleimide, as a monitor of the changes in the molecular organisation of the erythrocyte membrane which accompany band 3 cleavage. We report that the chymotrypsin treatment increases the rotational freedom of band 3, possibly due to conformational changes which disrupt its interaction with the underlying peripheral membrane proteins. We also show that chymotrypsin-treated erythrocytes undergo extensive endocytosis upon incorporation of exogenous fluorescently labelled phospholipid. We suggest that during the invasion process, digestion of band 3 by a chymotrypsin-like protease may induce a localised disruption of the erythrocyte membrane. This destabilised region of membrane may represent the site for the insertion of parasite-derived phospholipid, thus allowing the formation of the parasitophorous vacuole membrane.

28/7/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07684769 94070926

Immunochemical characterization and differentiation of two approximately 300-kD erythrocyte membrane -associated proteins of Plasmodium falciparum, PfEMP1 and PfEMP3.

Van Schravendijk MR; Pasloske BL; Baruch DI; Handunnetti SM; Howard RJ
Laboratory of Infectious Diseases, DNAX Research Institute, Palo Alto, California.

American journal of tropical medicine and hygiene (UNITED STATES) Nov 1993, 49 (5) p552-65, ISSN 0002-9637 Journal Code: 3ZQ
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Erythrocyte membrane-associated antigens of Plasmodium falciparum have been of long-standing interest as potential adherence receptors and vaccine candidates. We recently identified in trophozoite-stage infected erythrocytes a novel high molecular weight erythrocyte membrane -associated protein of P. falciparum , PfEMP3, defined by Western blotting with the rat monoclonal antibody 12C11. Genomic clone lambda 12.1.3 and cDNA clone p12.2 contain nucleic acid sequences encoding PfEMP3. Analysis of Malayan Camp strain parasites by sodium dodecyl sulfate-polyacrylamide gel electrophoresis on 5% gels revealed that PfEMP3, defined by Western blot, has the same relative molecular weight (M(r)) as the surface-exposed protein PfEMP1 defined by cell surface iodination. We show here that PfEMP3 is distinct from PfEMP1 by three criteria. First, 125I-labeled PfEMP1 was resolved from PfEMP3 by extended migration on 4% gels. Second, in two strains of P. falciparum in which 125I-PfEMP1 has a different M(r), PfEMP3 had the same M(r). Third, immunization studies were performed with fusion proteins derived from clones lambda 12.1.3 and p12.2. Although one rabbit, Rb 05.75, immunized with the PfEMP3-derived fusion protein beta gal12.1.3, produced a serum that strongly immunoprecipitated PfEMP1 as well as PfEMP3, most sera immunoprecipitated only PfEMP3. Furthermore, immunoprecipitation of PfEMP3 by Rb 05.75 serum was blocked by the glutathione S-transferase 12.1.3 fusion protein, whereas immunoprecipitation of PfEMP1 was unaffected. Therefore, we conclude that PfEMP1 and PfEMP3 are antigenically distinct.

28/7/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07566290 93295442
Cloning and characterization of a Plasmodium falciparum gene encoding a novel high-molecular weight host membrane-associated protein, PfEMP3.
Pasloske BL; Baruch DI; van Schravendijk MR; Handunnetti SM; Aikawa M; Fujioka H; Taraschi TF; Gormley JA; Howard RJ
DNAX Research Institute, Palo Alto, CA 94304.
Molecular and biochemical parasitology (NETHERLANDS) May 1993, 59 (1) p59-72, ISSN 0166-6851 Journal Code: NOR
Contract/Grant No.: AI-10645, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The rat monoclonal antibody, mAb 12C11, reacts with numerous proteins from mature asexual stages of Plasmodium falciparum. The largest is 315 kDa and is designated PfEMP3. A lambda gt11 expression library, generated from genomic DNA of Malayan Camp strain parasites, was screened with mAb 12C11. One positive clone, lambda 12.1.3, contained a 1.4-kb fragment in frame with the beta-galactosidase gene of lambda gt11. The deduced 455-amino acid sequence is a novel, highly charged sequence encoding two 15-amino acid repeats at the N-terminus followed by 27 repeats of 13 amino acids. The last 59 C-terminal residues are non-repetitive. Two in-frame stop codons at the 3' end of the DNA suggests that this DNA fragment encodes the C-terminus of the protein. Southern blotting with the cloned fragment identified two copies of this fragment per haploid genome in knob-positive, parasitized erythrocytes (K+PE). Both DNA fragments are absent from K - PE. Northern blotting of trophozoite-stage PE total RNA revealed mRNAs of 10, 4.4 and 2 kb in K+PE, but no hybridization with K - PE. Immune sera were elicited against the lambda 12.1.3 beta-galactosidase fusion protein and peptides generated from the predicted lambda 12.1.3 amino acid sequence. These sera and mAb 12C11 reacted specifically with PfEMP3 in Western blots of mature K+PE but not with K - PE. Rat and mouse sera against the recombinant protein produced an immunofluorescence pattern in fixed mature K+PE almost identical to the pattern produced by a monoclonal antibody against the knob-associated protein, Histidine Rich Protein 1. The same antibodies were immunofluorescence negative with fixed K - PE. Mouse antibodies against the recombinant protein reacted on immunoelectron microscopy with the erythrocyte membrane of K+PE, labeling knobs as well as the membrane between knobs. In contrast, a mAb against Histidine Rich Protein 1 reacted only under the electron dense material of knobs. We conclude that the lambda 12.1.3 clone encodes the C-terminal portion of the 315 kD PfEMP3 antigen and that PfEMP3 may be involved in knob formation or other perturbations of the erythrocyte membrane.

28/7/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07002362 92184117
The Pf332 gene of Plasmodium falciparum codes for a giant protein that is translocated from the parasite to the membrane of infected erythrocytes.
Mattei D; Scherf A
Unite de Parasitologie Experimentale, CNRS URA 361, Institut Pasteur, Paris, France.

Gene (NETHERLANDS) Jan 2 1992, 110 (1) p71-9, ISSN 0378-1119
Journal Code: FOP
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We studied the gene structure of the Plasmodium falciparum antigen 332 (Ag332). The gene size was estimated to be approx. 20 kb based on the large size of both the transcript found in mature asexual blood stage parasites and mung bean nuclease fragment generated from genomic DNA. Sequence analysis of genomic and cDNA clones representing different regions of the Pf332 locus showed that the gene product contains a large number of highly degenerated glutamic acid (Glu)-rich repeats (32% Glu). The gene shows dramatic restriction fragment length polymorphism in various P. falciparum isolates and was mapped to the subtelomeric region of chromosome 11. The recombinant 332 fusion protein reacts strongly with the human monoclonal antibody (mAb) 33G2, which is able to inhibit the cytoadherence of parasitized red blood cells on the melanoma cell line C32 and merozoite invasion in in vitro assays . The epitope recognized by this mAb is found frequently in the reported sequence. Ag332 monospecific antibodies were obtained by immunization of mice with a recombinant fusion protein. These antibodies react with a large parasite molecule with an apparent molecular size of 2500 kDa of trophozoite and schizont-infected erythrocytes on Western blot and by immunoprecipitation analysis. Immunofluorescence studies using a confocal microscope showed that Ag332 is exported from the parasite to the infected red blood cell membrane within large vesicle-like structures of about 1 micron diameter.

06717088 91275980
Plasmodium falciparum: analysis of the interaction of antigen Pf155/RESA with the erythrocyte membrane.
Ruangjirachuporn W; Udomsangpetch R; Carlsson J; Drenckhahn D; Perlmann P ; Berzins K
Department of Immunology, Stockholm University, Sweden.
Experimental parasitology (UNITED STATES) Jul 1991, 73 (1) p62-72, ISSN 0014-4894 Journal Code: EQP
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The location of the Plasmodium falciparum vaccine candidate antigen Pf155/RESA in the membrane of infected erythrocytes was analzyed by means of selective surface radioiodination and immunofluorescence of surface-modified cells. The lack of radiolabel in Pf155/RESA as well as its localization by immunofluorescence similar to that of the N-terminal region of erythrocyte band 3 suggests that the antigen is associated with the cytoplasmic phase of the erythrocyte membrane. In concordance with this, Pf155/RESA was detected by immunofluorescence on the surface of inside out membrane vesicles from P. falciparum-infected erythrocytes. Pf155/RESA from spent culture medium also bound to inside out membrane vesicles of normal erythrocytes as well as to cytoskeletal shells of such vesicles, but failed to bind to sealed right-side out membrane vesicles. Depletion of spectrin from the vesicles abolished antigen binding, suggesting that Pf155/RESA association with the erythrocyte cytoskeleton is mediated by spectrin.

28/7/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05242381 87107896
Inhibition of malaria parasite invasion of human erythrocytes by a lymphocyte membrane polypeptide.
Benzaquen-Geffin R; Milner Y; Ginsburg H
Infection and immunity (UNITED STATES) Feb 1987, 55 (2) p342-51, ISSN 0019-9567 Journal Code: GO7
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Extraction by boiling of the buffy coat of human blood yields a protein solution which inhibits the propagation of the human malaria parasite Plasmodium falciparum in culture with a 50% inhibitory dose of 105 micrograms of protein per ml. The inhibitory activity is associated exclusively with the lymphocytes and affects solely the invasion of erythrocytes by free merozoites. Boiled extracts of isolated lymphocytes had a 50% inhibitory dose of 22 micrograms/ml. Fractionation of surface-labeled or pronase-treated lymphocytes revealed that the antimalarial lymphocyte factor is associated with the intracellular aspect of the membrane fraction and is probably not involved in the host defense system against malaria. Further purification by salt extraction, ion-exchange chromatography, molecular gel filtration, and electroelution from lithium dodecyl sulfate-polyacrylamide gels resulted in 300- to 550-fold purification, i.e., a 50% inhibitory dose of 40 to 70 ng/ml. All inhibitory fractions contained a 48-kilodalton polypeptide which eluted from a gel filtration column as a 400-kilodalton species, implying multimeric association. Some 6,000 molecules of the 48-kilodalton polypeptide bind with high affinity to one merozoite, the free form of the parasite. The Kd of 0.1 to 0.5 nM for the binding of the 48-kilodalton polypeptide correlated well with the 50% inhibitory dose of 0.3 to 0.4 nM obtained with purified active antimalarial lymphocyte factor. We therefore suggest that the 48-kilodalton polypeptide partially purified from lymphocyte membranes is the antimalarial lymphocyte factor and that it exerts its inhibitory activity by binding to merozoites, thereby preventing their invasion into erythrocytes. The antimalarial lymphocyte factor or a polypeptide sequence thereof could serve for further probing of invasion at the molecular level.

28/7/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05071916 87304299
Plasmodium chabaudi malaria: red blood cells with altered membrane proteins in immune mice.
Wunderlich F; Helwig M
European journal of cell biology (GERMANY, WEST) Jun 1987, 43 (3) p499-500, ISSN 0171-9335 Journal Code: EM7
Languages: ENGLISH
Document type: JOURNAL ARTICLE

28/7/21 (Item 21 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

04829980 85170345
The relationship to knobs of the 92,000 D protein specific for knobby strains of Plasmodium falciparum.
Vernot-Hernandez JP; Heidrich HG
Zeitschrift fur Parasitenkunde (GERMANY, WEST) 1985, 71 (1) p41-51, ISSN 0044-3255 Journal Code: XZE
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A 92,000 D protein was identified associated with the membrane of host erythrocytes infected with the FCB1 Plasmodium falciparum strain from Colombia. The same protein was identified in the knob-forming Gambian (and the Malayan Camp) strain, but was not present in all the corresponding knobless strains. In the FCB1 strain as well as in the FCR3 strain the protein is synthesized during the ring-stage period. The cleavage products of the 92,000 D protein were investigated by peptide mapping following limited proteolytic digestion with Staphylococcus aureus V8 protease. The 92,000 D protein cleavage products from both the Colombian and the Gambian strains were identical. Moreover, both the proteins were sensitive to trypsin and chymotrypsin and also to treatment with neuraminidase. Enzymatic removal of the protein from the erythrocyte membrane by trypsin or chymotrypsin did not affect parasite maturation. The merozoites thus produced were fully invasive and the morphology of the knobs was unaltered. When the erythrocyte membrane was treated with trypsin before the time of synthesis of the 92,000 D protein, it was not possible to identify the protein in membranes of later stages of infected erythrocytes, indicating that the protein cannot be inserted into the membrane cytoskeleton compartment. Knobs, however, were formed more or less normally, suggesting that it is not the accumulation of this protein which products the knobs.

28/7/22 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

07218091 EMBASE No: 1998113661
Antibody reactivity to conserved linear epitopes of Plasmodium falciparum erythrocyte membrane protein 1 (PfEMP1)
Staalso T.; Khalil E.A.G.; Elhassan I.M.; Zijlstra E.E.; Elhassan A.M.; Giha H.A.; Theander T.G.; Jakobsen P.H.
T. Staalso, Centre for Medical Parasitology, Department of Clinical Microbiology, Copenhagen University Hospital, Copenhagen Denmark
AUTHOR EMAIL: tscmp@rh.dk
Immunology Letters (IMMUNOL. LETT.) (Netherlands) 1998, 60/2-3 (121-126)
CODEN: IMLED ISSN: 0165-2478
PUBLISHER ITEM IDENTIFIER: S0165247897001430
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 20

The Plasmodium falciparum erythrocyte membrane protein 1 (PfEMP1) family of protein antigens are involved in adhesion of P. falciparum infected erythrocytes to the capillary endothelium of the host. Antibodies to variable regions of these proteins, measured by

agglutination, correlates with clinical protection against falciparum malaria. In this study we investigated the occurrence of antibodies to conserved sequences of these very variable proteins in a population living in an area endemic for falciparum malaria. Using the ELISA method, we were able to measure an antibody response to three synthetic peptides derived from conserved regions of PfEMP1. The antibody responses to these peptides increased with age and were higher in individuals with asymptomatic P. falciparum infection compared to individuals presenting with fever attributable to falciparum malaria. This indicates that antibodies recognising the conserved regions of PfEMP1 arise upon exposure to the parasite, and that these may be involved in the development of protection against malaria. Antibodies to the Pfalhesin peptide of the human aniontransporter, band3, were measured by the same method. The magnitude of this antibody response did not correlate with neither age nor clinical protection.

28/7/23 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

05584124 EMBASE No: 1993352224
Immunochemical characterization and differentiation of two ~300-KD erythrocyte membrane-associated proteins of Plasmodium falciparum, PfEMP1 and PfEMP3

Van Schravendijk M.R.; Pasloske B.L.; Baruch D.I.; Handunnetti S.M.; Howard R.J.
Procept, Inc., 840 Memorial Drive,Cambridge, MA 02139 United States

American Journal of Tropical Medicine and Hygiene (AM. J. TROP. MED. HYG.) (United States) 1993, 49/5 (552-565)
CODEN: AJTHA ISSN: 0002-9637
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Erythrocyte membrane-associated antigens of Plasmodium falciparum have been of long-standing interest as potential adherence receptors and vaccine candidates. We recently identified in trophozoite-stage infected erythrocytes a novel high molecular weight erythrocyte membrane -associated protein of P. falciparum , PfEMP3, defined by Western blotting with the rat monoclonal antibody 12C11. Genomic clone lambda12.1.3 and cDNA clone p12.2 contain nucleic acid sequences encoding PfEMP3. Analysis of Malayan Camp strain parasites by sodium dodecyl sulfate-polyacrylamide gel electrophoresis on 5% gels revealed that PfEMP3, defined by Western blot, has the same relative molecular weight (M(r)) as the surface-exposed protein PfEMP1 defined by cell surface iodination. We show here that PfEMP3 is distinct from PfEMP1 by three criteria. First, sup 1sup 2sup 5I-labeled PfEMP1 was resolved from PfEMP3 by extended migration on 4% gels. Second, in two strains of P. falciparum in which sup 1sup 2sup 5I-PfEMP1 has a different M(r), PfEMP3 had the same M(r). Third, immunization studies were performed with fusion proteins derived from clones lambda12.1.3 and p12.2. Although one rabbit, Rb 05.75, immunized with the PfEMP3- derived fusion protein betagal12.1.3, produced a serum that strongly immunoprecipitated PfEMP1 as well as PfEMP3, most sera immunoprecipitated only PfEMP3. Furthermore, immunoprecipitation of PfEMP3 by Rb 05.75 serum was blocked by the glutathione S-transferase 12.1.3 fusion protein, whereas immunoprecipitation of PfEMP1 was unaffected. Therefore, we conclude that PfEMP1 and PfEMP3 are antigenically distinct.

28/7/24 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

130207051 CA: 130(16)207051r JOURNAL
Analysis of adhesive domains from the A4VAR Plasmodium falciparum erythrocyte membrane protein-1 identifies a CD36 binding domain
AUTHOR(S): Smith, Joseph D.; Kyes, Sue; Craig, Alister G.; Fagan, Toby; Hudson-Taylor, Diana; Miller, Louis H.; Baruch, Dror I.; Newbold, Chris I.
LOCATION: National Institute of Allergy and Infectious Diseases, Laboratory of Parasitic Diseases, National Institutes of Health, Bethesda, MD, USA
JOURNAL: Mol. Biochem. Parasitol. DATE: 1998 VOLUME: 97 NUMBER: 1,2
PAGES: 133-148 CODEN: MBIPDP ISSN: 0166-6851
PUBLISHER ITEM IDENTIFIER: 0166-6851(98)00145-5 LANGUAGE: English
PUBLISHER: Elsevier Science Ireland Ltd.
SECTION:
CA210001 MICROBIAL, ALGAL, AND FUNGAL BIOCHEMISTRY
CA203XXX Biochemical Genetics
IDENTIFIERS: Plasmodium variant surface antigen gene sequence, erythrocyte membrane protein 1 CD36 binding Plasmodium
DESCRIPTORS:
CD36(antigen)... Cell membrane... Erythrocyte... ICAM-1(cell adhesion molecule)... Plasmodium falciparum...
anal. of adhesive domains from A4VAR Plasmodium falciparum erythrocyte membrane protein-1 identifies CD36 binding domain
Glycolipoproteins...
VSG; anal. of adhesive domains from A4VAR Plasmodium falciparum erythrocyte membrane protein-1 identifies CD36 binding domain
CAS REGISTRY NUMBERS:
169443-42-9 amino acid sequence; anal. of adhesive domains from A4VAR Plasmodium falciparum erythrocyte membrane protein-1 identifies CD36 binding domain
166929-16-4 nucleotide sequence; anal. of adhesive domains from A4VAR Plasmodium falciparum erythrocyte membrane protein-1 identifies CD36 binding domain

28/7/25 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

130020241 CA: 130(3)20241k JOURNAL
A recombinant peptide based on PfEMP-1 blocks and reverses adhesion of malaria-infected red blood cells to CD36 under flow
AUTHOR(S): Cooke, Brian M.; Nicoll, Claire L.; Baruch, Dror I.; Coppel, Ross L.
LOCATION: Department of Microbiology, Monash University, Clayton, 3168, Australia
JOURNAL: Mol. Microbiol. DATE: 1998 VOLUME: 30 NUMBER: 1 PAGES: 83-90
CODEN: MOMIEE ISSN: 0950-382X LANGUAGE: English PUBLISHER: Blackwell Science Ltd.
SECTION:
CA201005 Pharmacology
IDENTIFIERS: recombinant peptide PfEMP1 malaria infected erythrocyte

adhesion CD36, Plasmodium falciparum erythrocyte membrane protein 1 peptide malaria
DESCRIPTORS:
Membrane proteins...
PfEMP-1 (Plasmodium falciparum erythrocyte membrane protein 1), (rC1-2(1-179)); recombinant peptide from PfEMP-1 inhibits adhesion of malaria-infected red blood cells to CD36 in relation to treatment
CD36(antigen)... Cell adhesion... Erythrocyte infection... Falciparum malaria... Plasmodium falciparum...
recombinant peptide from PfEMP-1 inhibits adhesion of malaria-infected red blood cells to CD36 in relation to treatment of complications of falciparum malaria

28/7/26 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

120296658 CA: 120(23)296658c PATENT
Pfemp3 malaria antigen, analogs, antibodies and uses thereof
INVENTOR(AUTHOR): Handunnetti, Shiroma M.; Howard, Russell J.; Pasloske, Brittan L.; Van, Schravendijk Marie R.
LOCATION: USA
ASSIGNEE: Schering Corp.
PATENT: PCT International ; WO 9403604 A1 DATE: 940217
APPLICATION: WO 93US7261 (930805) *US 927531 (920807)
PAGES: 110 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-015/30A; C07K-015/04B; C12P-021/08B; A61K-039/015B; A61K-039/395B; G01N-033/53B
DESIGNATED COUNTRIES: AU; BB; BG; BR; BY; CA; CZ; FI; HU; JP; KR; KZ; LK; MG; MN; MW; NO; NZ; PL; RO; RU; SD; SK; UA; VN DESIGNATED REGIONAL: AT; BE ; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG
SECTION:
CA215002 Immunochemistry
CA209XXX Biochemical Methods
CA212XXX Nonmammalian Biochemistry
IDENTIFIERS: malaria parasite membrane antigen Pfemp3, Plasmodium membrane antigen Pfemp3 cDNA
DESCRIPTORS:
Antibodies...
anti-idiotypic, to infected erythrocyte membrane antigen Pfemp3 of Plasmodium falciparum
Gene,animal...
cDNA, for erythrocyte membrane antigen Pfemp3 of Plasmodium falciparum, cloning of
Malaria...
diagnosis of, immunoassay for Pfemp3 antigen in
Deoxyribonucleic acid sequences,complementary...
for Pfemp3 antigen of Plasmodium falciparum
Immunoassay...
for Pfemp3 antigen of Plasmodium falciparum in diagnosis of malaria
Vaccines...
malaria, Pfemp3 antigen of Plasmodium falciparum as antigen in
Erythrocyte...
of malaria patients, Plasmodium falciparum antigens assocd. with, prepn. of monoclonal antibodies and cloning of cDNAs for
Protein sequences...

of Pfemp3 antigen of Plasmodium falciparum
Proteins,specific or class...
Pfemp3 (Plasmodium falciparum erythrocyte membrane protein 3), of Plasmodium falciparum, assocn. with erythrocyte membrane in malaria of, prepn. of monoclonal antibodies and cloning of cDNA for
Plasmodium falciparum...
Pfemp3 membrane antigen of, assocn. with erythrocyte membrane in malaria of, prepn. of monoclonal antibodies and cloning of cDNA for
Antigens...
Pfemp3, of Plasmodium falciparum, assocn. with erythrocyte membrane in malaria of, prepn. of monoclonal antibodies and cloning of cDNA for
Antibodies... Antibodies,monoclonal...
to infected erythrocyte membrane antigen Pfemp3 of Plasmodium falciparum
CAS REGISTRY NUMBERS:
154984-76-6 154984-78-8 154984-79-9 amino acid sequence of and cloning of cDNA for
154690-47-8 154758-30-2 epitope of Pfemp3 antigen of Plasmodium falciparum
154758-31-3P 154758-32-4P 154791-22-7P epitope of Pfemp3 antigen of Plasmodium falciparum, synthesis of, prpen. of antibodies to
154673-92-4 154758-29-9 in epitope of Pfemp3 antigen of Plasmodium falciparum
148451-14-3 154984-77-7 nucleotide sequence and cloning of

28/7/27 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

105059122 CA: 105(7)59122f JOURNAL
Membrane orientation and antigenic peptides of an immunoprotective 74 kDa Plasmodium knowlesi glycoprotein
AUTHOR(S): Schmidt-Ullrich, Rupert; Wallach, Donald F. H.; Monroe, Maureen M. T.
LOCATION: Dep. Ther. Radiol., Tufts-New England Med. Cent., Boston, MA, 02111, USA
JOURNAL: Mol. Biochem. Parasitol. DATE: 1986 VOLUME: 20 NUMBER: 1
PAGES: 15-23 CODEN: MBIPDP ISSN: 0166-6851 LANGUAGE: English
SECTION:
CA115002 Immunochemistry
CA114XXX Mammalian Pathological Biochemistry
IDENTIFIERS: glycoprotein Plasmodium infection erythrocyte membrane, malaria immunity antigen Plasmodium peptide
DESCRIPTORS:
Plasmodium knowlesi...
glycoprotein GP74 of, orientation of, in host membrane, peptides in relation to
Antigens...
glycoprotein, of Plasmodium knowlesi, orientation of, in host membrane
Malaria...
immunization against, with peptide of glycoprotein GP74 of Plasmodium knowlesi
Erythrocyte...
membrane of Plasmodium knowlesi-infected, glycoprotein GP74 orientation in, antigens of
Cell membrane...

of erythrocyte, glycoprotein GP74 incorporation in, in Plasmodium knowlesi infection, antigens in relation to
Peptides,biological studies...
of glycoprotein GP74, of Plasmodium knowlesi, antigen localization in, in host membrane
Glycoproteins,gp74...
of Plasmodium knowlesi, orientation of, in host membrane, peptides in relation to

28/7/28 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

011000427
WPI Acc No: 1996-497376/199649
New Plasmodium falciparum erythrocyte membrane proteins - used to develop products for the diagnosis, treatment or prevention of malaria parasite infections
Patent Assignee: AFFYMAX TECHNOLOGIES NV (AFFY-N)
Inventor: BARUCH D I; HOWARD R J; PASLOSKE B L
Number of Countries: 070 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9633736	A1	19961031	WO 96US5798	A	19960426	199649	B
AU 9658512	A	19961118	AU 9658512	A	19960426	199710	

Priority Applications (No Type Date): US 95430908 A 19950427
Cited Patents: 3.Jnl.Ref; WO 9403604
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9633736	A1	E	149	A61K-039/015	

Designated States (National): AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
Designated States (Regional): AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG

AU 9658512	A		A61K-039/015	Based on patent WO 9633736

Abstract (Basic): WO 9633736 A

A pure polypeptide comprising a Plasmodium falciparum (Pf) erythrocyte membrane protein 1 (PfEMP1) protein or a biologically active fragment or analog is new. Also claimed are: (1) an isolated nucleic acid encoding a PfEMP1 protein or a biologically active fragment; (2) a nucleic acid probe; (3) an expression vector comprising a nucleic acid segment encoding a PfEMP1 protein or a biologically active fragment is linked to a promoter sequence; (4) a recombinant host cell transfected with the expression vector of (3); and (5) an isolated antibody immunoreactive with a PfEMP1 polypeptide.

USE - The prods. can be used in the diagnosis , treatment or prevention of the onset of symptoms of a malaria parasite infection. In partic. the polypeptides can inhibit, block or reverse the sequestration of erythrocytes in patients suffering from malaria infections. The probe sequences of (2) may be used as primers in a method of identifying a P. falciparum parasite by amplifying nucleic acids from the parasite,generating a characteristics pattern of the amplified nucleic acids, and comparing the pattern to a known

characteristic pattern of amplified acids from a known P. falciparum strain (claimed).

Dwg.0/25

Derwent Class: B04; D16

International Patent Class (Main): A61K-039/015

International Patent Class (Additional): C12P-021/02

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